UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,195	12/19/2001	David Berd	1225/1D414US2	8483

28977 7590 05/24/2004

MORGAN, LEWIS & BOCKIUS LLP
1701 MARKET STREET
PHILADELPHIA, PA 19103-2921

EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,195	BERD, DAVID	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *08 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *2 and 6-24* is/are pending in the application.

4a) Of the above claim(s) *9-21,23 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *2,6-8 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The Amendment filed March 8, 2004 in response to the Office Action of September 3, 2003 is acknowledged and has been entered. Previously pending claims 1, 4-5 have been cancelled, claims 2 and 6-7 have been amended and new claims 22-24 have been added. Newly added claims 23-24 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 2, 6-8, 22 are currently being examined.

2. Since applicant has elected Group I a method of treating adenocarcinoma comprising administering to a human a composition comprising a therapeutically effective amount of a hapten modified autologous human tumor cell substantially in a no growth phase and an adjuvant, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, the embodiments of claims 23-24 directed to the method of claim 1 and further comprising eliciting an inflammatory immune response against said carcinoma, further comprising eliciting a delayed-type hypersensitivity to said carcinoma have been withdrawn from consideration as being directed to a non-elected invention and only the originally claimed invention is being examined. See 37 C.F.R. ' 1.142(b) and M.P.E.P. ' 821.03. Newly submitted claims 23-24 are directed to inventions that are independent or distinct from the invention originally claimed because they are not drawn to treatment *per se* and differ at least in objectives, response variables, and criteria for success.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The following rejections are being maintained and new rejections are applied in view of the amendments of the claims:

Claim Rejections - 35 USC 112

5. Claims 2, 6-8 remain rejected and newly added claim 22 is rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed September 3, 2003, Section 8, pages 4-7.

Applicant argues that amendment of the claim to recite "substantially in a no growth state" obviates the grounds of rejection. Applicant further argues that the specification makes clear that "substantially in a state of no growth refers to cells which are not going to grow and divide after administration such that they are "cells that will not divide *in vivo*" and points to page 10, lines 17-20. The argument has been considered but has not been found persuasive. A review of page 10, lines 17-20 reveals that the phrase "cells that will not divide *in vivo*" is not drawn to the term "substantially" but is drawn to "cells in a state of no growth". Further, while applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term, In re Hill, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). Although not defined in the specification, the term "substantially" is understood by the art (as defined by Webster's II New Riverside University Dictionary, 1994, Houghton Mifflin Company, Boston, MA, p. 1155) to mean "being of considerable....amount", that is, most but not all of something. The issue of division or non-division is absolutely critical to cancer therapy. Either cells will or will not grow and divide. If they are substantially in a no growth state then according to Webster, not all of them are in a no growth state and Applicant's teaching that cells that are "substantially in a state of no growth" will not grow and divide is repugnant to the usual meaning of the term "substantially".

Applicant further argues that the specification notes that methods for suspending cells in a state of no growth were well-known in the art and points to

lines 21-24 of page 10. The argument has been considered but has not been found persuasive because as previously set forth, other than conventional irradiation, no methods of suspending the cells in a state of no growth are taught.

Applicant further argues that the specification at page 21, lines 1-5 discloses that although it is theoretically possible that injected tumor cells could grow in a patients skin, this has not been observed in more than 200 patients injected with vaccines prepared similarly to the vaccine of the present invention .....and growth is considered a very remote possibility. The argument has been considered but has not been found persuasive as the vaccine of the present invention was prepared using irradiated cells.

The arguments have been considered but have not been found persuasive and the rejection is maintained.

6. Claims 2, 6-7 remain rejected and newly added claim 22 is rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed September 3, 2003, Section 9, pages 7-8.

Applicant argues that Hoover and the '551 patent merely teach that BCG is an adjuvant that can be used but do not teach that only BCG can be used as an adjuvant and the cells used in those methods are different that the cells used in the instant invention. and the specification discusses additional adjuvants which can be used in the methods of the invention and other adjuvants are amply supported in the specification.

The argument has been considered but has not been found persuasive because both Hoover et al and the '551 patent specifically teach that the appropriate adjuvant was a critical condition of success of the immunotherapy using irradiated tumor cells, although the instantly claimed colon cells are indeed

different from the cells of Hoover et al because they are haptenized, this does not abrogate the effectiveness of BCG adjuvant nor suggest that "any" other adjuvant would function to effectively produce an effective immune response. The critical nature of the adjuvant is also disclosed in the '551 patent. However, although the cell type was different, this does not abrogate the clear effectively of the BCG adjuvant nor suggest that "any" other adjuvant would function to effectively produce an effective immune response. Further, in light of the teaching of Livingston et al that immune response was not induced unless BCG was added to the vaccine, although the vaccine used was not autologous colon tumor cells, this clearly demonstrates the critical nature of the adjuvant. Given that no other adjuvant has been taught in either the specification or the art of record that is useful for producing an effective tumor cell vaccine, the art of record calls into serious question the breath of the claims as currently constituted and for the reasons of record no one of skill in the art would believe it more likely than not that the invention will function as broadly claimed. Applicant's arguments have not been found persuasive and the rejection is maintained.

Claim Rejections - 35 USC 103

7. Claims 2, 6-8 remain rejected and claim 22 is rejected under 35 USC 103 for the reasons set forth previously in the paper mailed September 3, 2003, Section 11, pages 3-5.

Applicant argues that Examiner has not provided either a suggestion or motivation either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, has not demonstrated that there is a reasonable expectation of success or has suggested all of the claim limitations.

In particular, Applicant argues that Hoover et al do not teach haptenization and the '551 is silent as to melanoma and Examiner's finding of obviousness is based on impermissible hindsight. The argument has been considered but has not been found persuasive because some degree of hindsight is permissible in making rejections under 35 USC 103. Clearly it was well known in the art that irradiated human colon cancer cells in combination with BCG was an effective anti-cancer vaccine as taught by Hoover et al and that haptenization of tumor cells leads to increased infiltration of T lymphocytes into the tumor mass (which the '551 patent specifically teaches is a significant advance in the art), which is a prerequisite for tumor destruction by the immune system, as taught by the '551 patent. Contrary to the assertion of Applicant that the rejection is based on impermissible hindsight, the references teach not only the suggestion but also the means and motivation to successfully treat colon adenocarcinoma using haptenized irradiated colon cancer cells in conjunction with BCG. The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Applicant further argues that in light of the foregoing arguments, it is clear that there was no reasonable expectation of success in combining the references. The argument has been considered but has not been found persuasive considering the clear fact that even without haptenization the colon cancer vaccine of Hoover et al was successful. It would have been expected, given the teach of the '551 patent

that the efficiency of the vaccine process for the treatment of colon cancer would have been increased with the conjugation of the cells to DNP.

Applicant further argues that the combined references do not teach or suggest all of the claim elements since one teaches haptenized melanoma cells and the other teaches unhaptenized colon cancer cells and the two cannot be harmonized. The argument has been considered but has not been found persuasive for the reasons of record, the prior art references make obvious the claimed invention.

New Grounds of Rejection

Claim Rejections - 35 USC 112

8. Claims 2, 6-8 and 22 are rejected under 35 USC 112, second paragraph as indefinite because claim 2 is drawn to a method of treating an adenocarcinoma comprising administering a hapten modified autologous human tumor cell, wherein the patient suffers from a malignant tumor of the same type as said tumor cell wherein said adenocarcinoma is colon carcinoma. The claim is confusing because it is not clear whether the tumor type is adenocarcinoma, of which numerous types are known, or whether the tumor type referred to is colon adenocarcinoma. The rejection can be obviated, for example by amending claim 2 to recite "a method for treating cancer wherein said cancer is colon adenocarcinoma comprising administering to a human.....amount of a hapten modified autologous human colon adenocarcinoma cell.....".

9. Claims 2, 6-8 and 22 are rejected under 35 USC 112, first paragraph as the specification does not contain a written description of the claimed invention. The limitation of treating an adenocarcinoma comprising administering a hapten modified autologous human tumor cell, wherein the patient suffers from a

malignant tumor of the same type as said tumor cell wherein said adenocarcinoma is colon carcinoma as recited in claim 2 has no clear support in the specification and the claims as originally filed. The claims as written are drawn to a method of treating colon adenocarcinoma with a hapten modified autologous human tumor cell that is an adenocarcinoma cell, wherein there is no limitation that the tumor cell administered is an colon adenocarcinoma cell. The subject matter claimed in claims 2, 6-8 and 22 broadens the scope of the invention as originally disclosed in the specification.

10. Claims 2, 6-8 and 22 are rejected under 35 USC 112, first paragraph because the specification, while being enabling for the claimed method comprising administering haptenized autologous colon cancer cells, does not reasonably provide enablement for said method comprising administering haptenized autologous adenocarcinoma cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are drawn to a treating an adenocarcinoma comprising administering a hapten modified autologous human tumor cell, wherein the patient suffers from a malignant tumor of the same type as said tumor cell wherein said adenocarcinoma is colon carcinoma. This includes the treatment of colon adenocarcinoma with any adenocarcinoma cell. The specification teaches the treatment of colon adenocarcinoma with haptenized colon cancer cells. One cannot extrapolate the teaching of the specification to the scope of the claims because of the art recognized heterogeneity of cancer cell types. No one of skill in the art would believe it more likely than not that an adenocarcinoma cell other than a colon cancer adenocarcinoma cell would possess the surface antigens that are

expressed on colon cancer cells in an amount sufficient to stimulate an immune response of T-cells that would infiltrate the tumor. The specification provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the claimed invention would function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

11. Misspellings in the specification have been noted, for example, on page 10, line 18 wherein "sate" is disclosed. Applicant is required to check the specification and note where all such informalities occur. Appropriate correction is required.

12. All other objections and rejections recited in the paper mailed September 3, 2003 are withdrawn.

13. No claims allowed.

14. This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier.

Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal from, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

15. Applicant's amendment necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

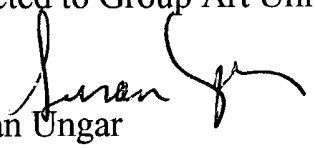
A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at 571-272-0841. The fax phone number for this Art Unit is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.



Susan Ungar
Primary Patent Examiner
May 19, 2004